REMARKS

Claims 1-8 and 44-57 are under examination are under examination. Claims 1, 2, 5, 7, 44, 50, 52, and 56 have now been amended.

Applicants respectfully assert that all amendments and new claims are supported by the original disclosure and do not introduce new matter. Moreover, Applicants further respectfully assert that the amendments merely clarify the scope of the claims.

Applicants acknowledge the Examiner's withdrawal of the earlier rejection of claims 1-8 and 44-49 under 35 U.S.C. 102(b) as being anticipated by Morimoto et al. (J. Bio. Chem., 1990, 265(4): 1933-1937), and as evidenced by Morimoto et al. (Proc. Natl. Acad. Sci. U.S.A., 1989: 86: 3389-3393) and rejection of claims 1-8 and 44-49 under 35 U.S.C. 103(a) as being unpatentable over Vaccaro et al. (FEBS 1993, 336(1): 159-162) in view of the teachings of O'brien et al. (W09503821A1). Applicants appreciate the Examiners help with this matter.

The rejection of claims 1-8 and new claims 50-57 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained in light of the earlier response that claims have been amended to limit the inner leaflet component to a phospholipids selected from the group consisting of phosphatidylserine, phosphatidylethanolamine, and structural analogs thereof.

The response states that applicants have provided sufficient detailed examples in the specification showing peptides comprising less than the full amino acid protein depicted in SEQ ID NO:1 and 2. The U.S. Patent Office clearly does not require a description of every embodiment for peptide claims and that while protein chemistry taken as a whole may be unpredictable, particular embodiments are patentable. The Examiner acknowledges that the applicants have provided sufficient detail of particular patentable embodiments. The Examiner also acknowledges that because of the unpredictability of living processes, generic biological claims inherently must cover inoperative members of the class. This is not fatal to the claim if a person skilled in the art can recognize which species are operative and which are not, especially if functional limitations are used to exclude inoperative members. In the present case, inoperative

members are specifically excluded through the functional limitations that the polypeptide must retain plasma-membrane affinity.

The Examiner contends that because claims 1-8 still recite a prosaposin-related polypeptide comprising an amino acid sequence substantially identical to and having 80% sequence identity to SEQ ID NO. 1 or 2. Furthermore, new claims 50-57 recite "a prosaposin-related polypeptide", which encompass polypeptides that are at least 80% identity to the amino acid sequence set forth in SEQ ID NO.1 and fragments thereof (see specification page 4). As stated in the previous office action, the instant specification fails to provide sufficient descriptive information such as a core structure that is required for the function (i.e. retain plasma membrane affinity) and is common to the genus of the sequences that are at least 80% identical to SEQ ID NO.1 or 2 and fragments thereof. Therefore, applicants are claiming a genus of homologs and fragments that are only characterized by their functional characteristics i.e. retain plasma membrane affinity. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factors present in the claim are recitation of "80% sequence identity", "a prosapsin-related polypeptide" and retains plasma membrane affinity.

The rejection of claims 1-8 and new claims 50-57 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent comprising an anionic phospholipid, particularly phosphatidylserine and a prosaposin polypeptide of SEQ ID NO.1 or SEQ ID NO.2, does not reasonably provide enablement for an agent comprising any and all inner leaflet component, and any and all prosaposin-related polypeptide of an amino acid sequence that is at least 80% identical to SEQ ID NO.1 or 2 is maintained.

Applicant's arguments have been carefully considered but are not found persuasive. Because applicant fails to provide adequate written description for a polypeptide that is at least 80% identical to SEQ ID NO. 1 or 2, and a prosaposin-related polypeptide for the reasons set

forth above, one skilled in the art would not know how to identify the species encompassed by the claimed genus of polypeptide, as such one would not know how to make the broad class of a polypeptide that is at least 80% identical to SEQ ID NO. 1 or 2, and a prosaposin-related polypeptide that possess the required function i.e. retain plasma-membrane affinity. Therefore, the rejection is proper and maintained.

Applicants respectfully traverse this rejection in light of the showing of working examples in the specification, the predictability of the art for the claim scope, the correlation of working examples of the claimed invention, the correlation of working examples in the prior art to the claimed invention, and the correlation of animal models to the disease.

Applicants have provided sufficient detailed examples in the specification showing peptides comprising less than the full amino acid protein depicted in SEQ ID NO:1 and 2. The U.S. Patent Office clearly does not require a description of every embodiment for peptide claims and that while protein chemistry taken as a whole may be unpredictable, particular embodiments are patentable.

Applicants believe that the Examiner is wrongly inserting their own opinion into the case as to what is an adequate written description. It is obvious from the over 1400 issued patents described precisely as the present claims that it is well accepted in the art to describe variants as the applicants have in the present application..

It is well-known in the art that the proteins of the invention may be altered in various ways including amino acid substitutions, deletions, truncations, and insertions. Methods for such manipulations are generally known in the art and such variations are easily determined using well known laboratory procedures..

Applicants have provided sufficient detail of particular patentable embodiments and a person skilled in the present art can easily ascertain the sequences that fall within the scope of the present claims.

Nonetheless, Applicants have now amended the claims to further define the present invention and to provide that the amino acid sequence is substantially identical to the amino acid

sequence set forth in SEQ ID NO:1/2 having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:1/2, wherein the polypeptide comprises a biologically active portion of a (pro)saposin polypeptide comprising at least 25 contiguous amino acids present in a (pro)saposin polypeptide and retains plasma-membrane affinity.

As stated above, Applicants contend that the claims, as now amended, are fully enabled. Applicants respectfully submit that the specification provides adequate direction to those skilled in the art and that the disclosure would not require undue experimentation.

Thus, is respectfully submitted that the present specification fully meets the requirements of 35 U.S.C. 112 and withdrawal of these rejections is respectfully requested.

The Examiner has maintained the rejection of claims 1-3, 44-47 and new claims 50-52 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 16, 17, 21 and 22 of U.S. Patent No. 6,872,406 in view of Vaccaro et al. (FEBS Lett. 1994, 349: 181-186, IDS).

The Examiner has maintained the provisional rejection of claims 1-3, 44-47 and new claims 50-52 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16, 17, 21 and 22 of copending Application No. 10/967,921 in view of Vaccaro et al. (FEBS Lett. 1994, 349: 181-186, IDS) is maintained.

Applicants assert that they will file a Terminal Disclaimer (and filing fee) assuring that the present application and co-pending Application No. 10/967,921 will expire at the same time if conflicting claims are issued. The filing of this Terminal Disclaimer should render moot the double patenting rejection.

New Grounds of Rejections

The Examiner has rejected claims 1-8, 44-49 and new claims 50-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaccaro et al. (FEBS 1993, 336(1): 159-162) in view of the teachings of O'Brien et al. (WO9503821A1), as evidenced by Vaccaro et al. (FEBS, 1994, 349: 181-186, IDS) .

Applicants point out that the teachings of Vaccaro and O'Brien show forming liposomal vesicles and then adding saposin C to the formulation, resulting in a surface interaction of the protein with the vesicles. A lipid/saposin vesicle formed by this method will not function the same and will not exhibit anti-tumor activity as with the vesicles of the present invention.

In Vaccaro, the reference shows that lipids are mixed together to form the vesicles first and then the formed vesicles are mixed with saposin C. Compositions formed by this method yield saposin C interacting with the surface of the formed membranes but that is not the interaction of the present invention. While they may achieve activation of the enzyme, they do not form a complex with the saposin integrated into the vesicle.

The present invention provides for mixing both the saposin C and the lipids together at the same time in an acidic environment to form the integrated saposin C vesicles. The claims have now been amended to clarify this important feature showing that the prosaposin related polypeptide and the inner leaflet component are combined in an acidic buffer and then treated together to form a nanovesicle exhibiting anti-tumor activity.

Support for these amendments can clearly be seen from the details of Example 2.

Applicants contend that nothing in the cited references would teach or suggest the claims, as now amended and would not have been obvious to those skilled in the art.

Thus, it is respectfully submitted that the present specification fully meets the requirements of patentability and withdrawal of the rejection under section 103 is respectfully requested.

Claim Rejections - 35 USC § 112, 2nd paragraph

Claims 2, 5, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the limitation "the biocompatible phospholipid" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 2 has now been amended to correct the deficiency in antecedent basis for this claim.

Claim 5 recites the limitation "fusogenic polypeptide" in claim 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 5 has now been amended to correct the deficiency in antecedent basis for this claim.

Claim 7 recites the limitation "the biologically active portion of prosaposin polypeptide" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 has now been amended to correct the deficiency in antecedent basis for this claim.

Conclusion

In light of the amendments and remarks made herein, it is respectfully submitted that the claims currently pending in the present application are in form for allowance. Accordingly, reconsideration of those claims, as amended herein, is earnestly solicited. Applicants encourage the Examiner to contact their representative, Stephen R. Albainy-Jenei at (513) 651-6839 or salbainyjenei@fbtlaw.com. The Commissioner for Patents is hereby authorized to charge any deficiency or credit any overpayment of fees to Frost Brown Todd LLC Deposit Account No. 06-2226.

Respectfully submitted,

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